



# NEURON-SPECIFIC ENOLASE AS A MARKER OF PERINATAL CENTRAL NERVOUS SYSTEM DAMAGE IN CHILDREN WITH BRONCHIAL ASTHMA

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## ABSTRACT

*One of the most common childhood diseases that affects the quality of life of patients and their families, which in severe cases leads to disability, is bronchial asthma (BA). The results of recent studies show that the majority of children with bronchial asthma have a history of perinatal damage to the central nervous system (CNS), which increases the risk of developing bronchial asthma in children of preschool age by 3.4 times. Particular attention of researchers is drawn to the study of the diagnostic and prognostic significance of biochemical markers of neuronal damage in fetuses and newborns, in particular, neuron-specific enolases. In this regard, it is of interest to study the level of neuron-specific enolase in children with asthma who suffered perinatal damage to the central nervous system.*

**KEYWORDS:** bronchial asthma, perinatal damage, central nervous system, newborns, adolescents, neuron-specific enolase.

Bronchial asthma is a common chronic inflammatory allergic disease of the respiratory system in childhood. Disability among the child population due to allergic diseases is formed mainly due to bronchial asthma, so the priority task is to find methods for predicting the development of severe forms and uncontrolled course of the disease [6,8,13,19].

According to research data, more than 80% of all cases of bronchial asthma (BA) have their origins at an early age, manifesting themselves in repeated episodes of broncho-obstructive syndrome against the background of acute respiratory viral infections [6,7,15].

Various adverse effects in the ante- and postnatal period can contribute to the sensitization of the child's body, change

the functional activity of the neuroimmune-endocrine system, which affects the development of allergic inflammation and bronchial hyperreactivity [7,8].

Recently, an opinion has increasingly been expressed about the serious contribution of hypoxic damage to the central nervous system (CNS) and prematurity in the genesis of bronchial asthma. Hypoxia and prematurity are factors in the imperfection of the newborn's immune response, leading to frequent infectious diseases that disrupt the neurogenic regulation of the bronchi [8,13,21]. Some studies have noted a correlation between the depth of CNS damage and the severity of BA symptoms caused by more severe neuro-immune-endocrine imbalance [6,7,16].

Neurological and psychopathological disorders that develop as a result of perinatal central nervous system lesions (PCNSL) naturally close the vicious circles of AD pathogenesis, limiting

the patient's adaptive capabilities throughout life. In this regard, the study of clinical and dynamic features of psychoneurological disorders in children with BA is a very urgent task, as it can help improve methods of prevention and treatment of this disease [7,8,20].

It has been proven that perinatal damage contributes to the frequent development of bronchial obstruction in children in the first years of life [9,18]. However, in order to fully reveal the pathogenetic mechanisms of the formation of asthma in children, a comprehensive examination using modern diagnostic methods is necessary [11,13].

In this regard, special attention of researchers has been drawn to the study of the diagnostic and prognostic significance of biochemical markers of neuronal damage in fetuses and newborns [2,3,5,12,14,16]. These markers include neurotrophins and neurospecific proteins that play an important role in brain development. One of the markers of neuronal damage is neuron-specific enolase (NSE), which is localized in the cytosol of neurons and endocrine cells and is found in the blood when they are destroyed [1,3,4,7,9,15].

Enolase is a glycolytic enzyme. In other words, it is involved in the breakdown of carbohydrates. In this case, energy is released, which is used to support various life processes. This enzyme is present in all cells, but different tissues contain different species (isoforms). So, one of them is neuron-specific enolase (NSE), which is localized in neurons [1,2,10,12,17].

It has been shown that an increase in its level in premature newborns who have suffered asphyxia or cytomegalovirus



infection is an unfavorable factor in relation to the prognosis of further psychomotor development [1,3,5,10,16,18].

Morozova A.Yu. et al. (2019) found that in full-term newborns with intrauterine growth retardation of II-III degrees, not only the content of neuron-specific in the blood is increased by 2-2.5 times enolase, but also a low level of neurotrophic growth factor is determined [10,12].

All of the above once again proves the need for an in-depth study of the course of bronchial asthma in children at the present stage with clarification of the role of perinatal damage to the nervous system and, especially, the content of neuron-specific drugs in the blood, enolase (NSE) with the development of timely diagnostic methods.

**THE PURPOSE OF THE STUDY** was to study the content of neuron-specific enolase in children with bronchial asthma as a predictor of perinatal damage to the central nervous system.

**MATERIALS AND METHODS.** The study was conducted on the basis of the pulmonology department of the regional children's multidisciplinary medical center Samarkand. The study is based on data from a comprehensive examination of 48 children with bronchial asthma (BA) aged 5-11 years. Observation of patients began with a detailed analysis of the perinatal history. The anamnestic data of the examined children was documented by an extract from the maternity hospital.

When selecting patients for the study, the inclusion criteria were all children diagnosed with asthma aged 5 to 11 years. Exclusion criteria included children under 5 and over 11 years of age; concomitant gross somatic pathology and organic neurological symptoms. The control group consisted of 18 practically healthy children of identical age. The criteria for selecting children into the control group were the absence of

active complaints during a targeted survey of children and their parents. Clinical neurological examination revealed no signs of organic damage to the nervous system; medical documentation data did not contain information about the pathology of the perinatal period, inflammatory and traumatic diseases of the nervous system.

The level of NSE, a highly specific marker of neuronal damage, was determined by enzyme-linked immunosorbent assay (ELISA) using "Nikom Can kits Ag NSE EIA" (Sweden) according to the manufacturer's instructions. The ELISA results were taken into account photometrically using a Stat photometer Fax » 1904+ USA. Before the analysis, it was recommended to adhere to the following preparation rules: refrain from intense physical activity for 2-3 days; Do not eat fatty foods for 1 day. To determine NSE concentration, blood was taken from the antecubital vein. The data specified by the developer company were used as normal values; NS E 13.0 µg/l was considered the upper limit of normal values.

**RESEARCH RESULTS.** During the study, the observed children with BA were divided into 2 groups: the first (main group) group consisted of 25 children with BA, whose perinatal history contained indications of prenatal, intranatal or postnatal risk factors for the development of perinatal CNS damage.

The second group (comparison group) - 23 children with asthma without concomitant damage to the perinatal central nervous system. The children's mothers were healthy and the pregnancy proceeded without complications.

The distribution of children by age and gender in the observation groups showed their comparability (Table 1). In both groups of children with asthma, boys slightly predominated, amounting to 54.2%, and the average age of the examined children with asthma was 7.75±0.99 years.

**Table 1**  
**Gender and age characteristics of the examined children**

Sign	Main group (n=25) abs. /%	Comparison group (n=23) abs. /%	Control group (n =18) abs. /%
Boy, abs. /%	14; 56	12; 52.2	10; 55.6
Girl, abs. /%	11; 44	11; 47.8	8; 44.4
Average age, years	7.8±1.1	7.65±0.89	7.65±1.12

Analysis of the perinatal history showed in the main group of children with BA the predominance of low birth weight among prenatal factors (RR=0.521;  $\chi^2=10.6$ ; P<0.05), severe toxicosis in the mother (RR=0.642;  $\chi^2=12.9$ ; P<0.01), fetoplacental insufficiency (RR=0.565;  $\chi^2=12.7$ ; P<0.01). Among the intrapartum factors, bleeding was noted with placenta previa (RR=0.792;  $\chi^2=19.1$ ; P<0.001), prolonged difficult labor (RR=0.811;  $\chi^2=15.4$ ; P<0.01), as well as fetal hypoxia during labor (RR=0.621;  $\chi^2=13.7$ ; P<0.05). Postnatal risk factors were represented mainly by mechanical ventilation after the birth of the child (RR=0.621;  $\chi^2=14.9$ ; P<0.05), neonatal seizures (RR=0.741;  $\chi^2=17.9$ ; P<0.01).

Analysis of delivery and the condition of the child at birth in the observation groups showed that of the total number of children in the main group, 11 were born naturally (44%), and 14 (56%) were delivered by cesarean section, the indications for which were the lack of effect from treatment of gestosis and chronic placental insufficiency. Whereas in the comparison group these indicators were 22 (95.7%) and 1 (4.3%), respectively. In the control group of children, physiological birth was noted in 100% of cases (Figure 1). The average Apgar score in children in the control group was 8±0.87 points, while in the main group (6±0.77 points) it was significantly lower than even in the comparison group (7.87±0.97 points).

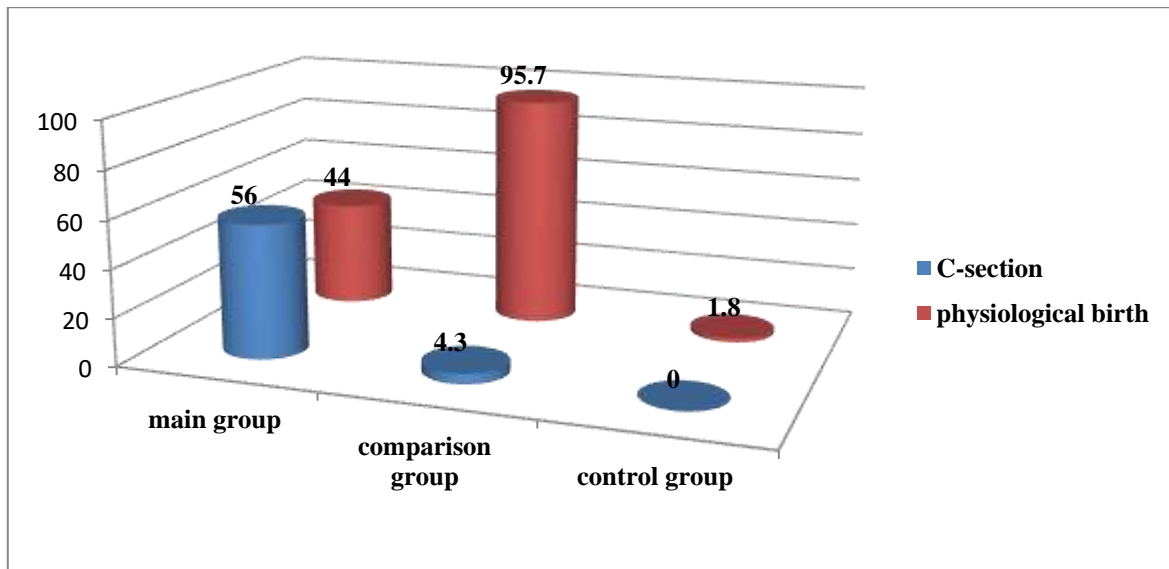


Figure 1. Peculiarities of delivery of mothers in observation groups (%)

The average weight and height of children with asthma at birth in the study group was 3220.0±138.6 g and 53.7±0.8 cm, respectively, while the body weight and height of children in the main group (2976.0±178.9 g and 50.9±0.56 cm) were significantly lower than in the comparison group

(3460.2±133.4 g and 54.7±0.4 cm) (P<0.05). In the control group of children, body weight and height at birth were (3524.2±143.4 g and 55.3±0.7 cm) (Figure 2).

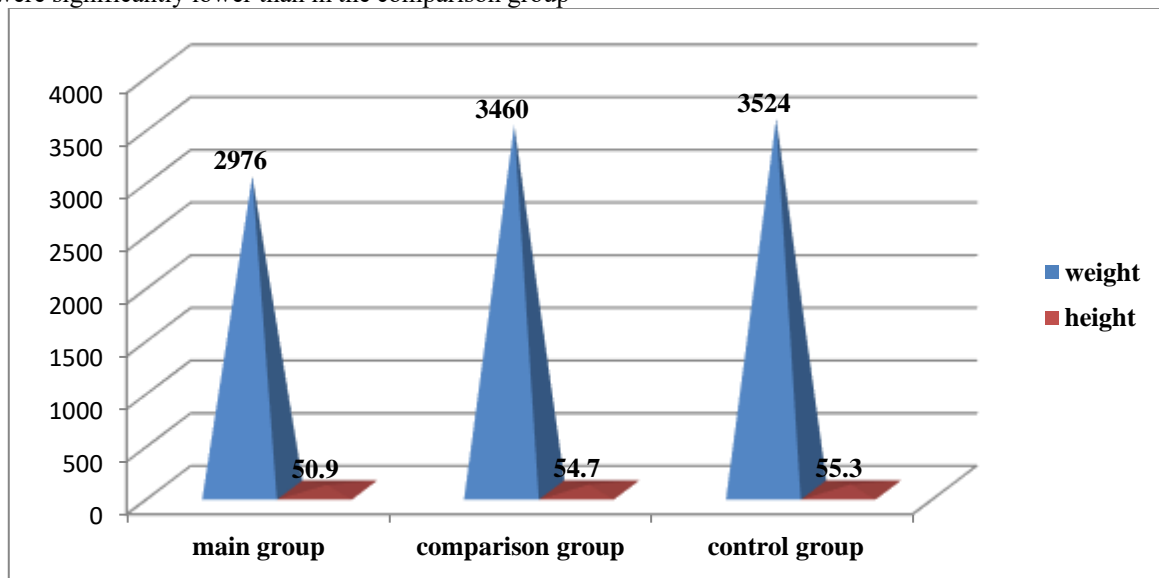


Figure 2. Weight (grams) and height (cm) of children at birth in observation groups

And an analysis of the complaints of children in both observation groups showed that the main complaints during hospitalization of patients in the hospital were expiratory shortness of breath (64.9% and 49.4% in the main and comparison groups, respectively). Dry cough was significantly more common in the main group - 67.3%, while productive cough, on the contrary, was significantly more common in the comparison group - 53.4% and was effective in nature. An increase in expiratory shortness of breath and wheezing at the beginning of the disease was recorded in 42.5% of cases in children with asthma who had a history of perinatal central nervous system damage. Also, patients in the main group were characterized by

complaints of decreased appetite, weakness, fatigue, lack of air, and symptoms of intoxication - 66.8% of cases. It should be noted that in more than half of the cases these complaints were clearly expressed.

A study of the syndromic consequences of perinatal hypoxic damage to the central nervous system in children of the main group revealed various speech disorders (19; 76%), autonomic dysfunction (15; 60%) and hyperreactivity and attention deficit syndrome (20; 80%). Some children in the main group had neuroses and neurotic reactions (7; 28%), as well as a neurogenic bladder (6; 24%) (Figure 3).

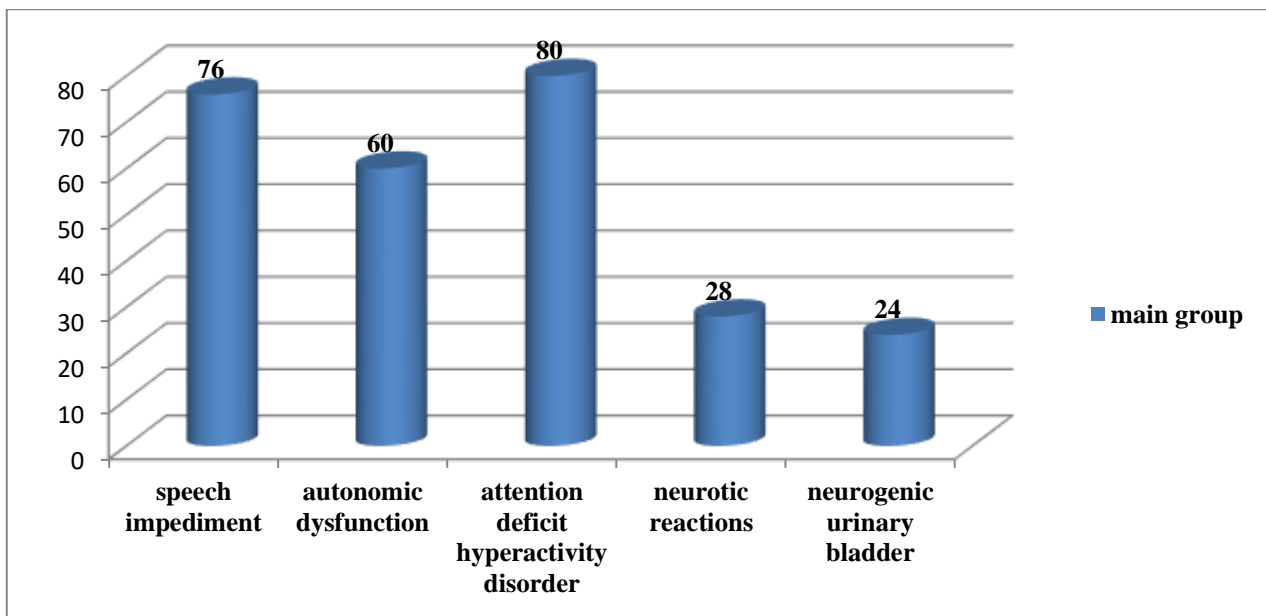


Figure 3. Characteristics of Neurological Syndromes in the main group of children with asthma

At a further stage, the level of neuron-specific enolase in study groups. It was found that in healthy children ( $11.1 \pm 1.9 \mu\text{g/l}$ ) and children with asthma from the comparison group ( $12.1 \pm 0.9 \mu\text{g/l}$ ) the level of neuron-specific enolase was within normal values. Whereas in the group of children with asthma against the background of the consequences of perinatal damage to the central nervous system, this marker was almost 1.9 times higher than the values in the control group and 1.7 times higher than the value obtained in patients from the comparison group, amounting to  $21.1 \pm 0.54 \mu\text{g/l}$ .

As a result, it was found that, regardless of the severity of the identified neurological syndromes, in the main group of patients there was an inverse correlation between the signs of a strong close connection -  $r = 0.699$  ( $P < 0.01$ ).

Thus, the data obtained indicate that the level of neuron-specific enolase in children with bronchial asthma who suffered perinatal CNS damage is significantly higher not only in comparison with healthy peers, but also with children suffering from asthma without signs of perinatal CNS damage. The data obtained can be used not only as important predictors of the prognosis of the severity of bronchial asthma and concomitant conditions, but also, most importantly, to evaluate the effectiveness of the therapy including correction of the neurological status against the background of pathogenetic therapy of the underlying disease.

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